## Remarks

In a previous Office Action/Restriction Requirement dated June 18, 2007, the Examiner noted that claims 1 - 20 are subject to restriction in that as filed, they allegedly cover nine (9) independent and distinctly methods of treating a variety of different unrelated medical disorders caused by different unrelated biological pathways whose treatment thereof would therefore constitute separate, unrelated inventions. In particular, the Examiner required an eight-way restriction in accordance with 35 U.S.C. 121 as follows:

1) Claims 1 – 7 drawn to a method of treating a patient for sleep disorders comprising the administration of the claimed compounds of the invention.

2) Claims 8,9,16 and 17 drawn to a method of treating a patient for anxiety disorders through the administration of the claimed compounds

3) Claims 8, 10, 16 and 17 drawn to a method of treating a patient for mood disorders.

4) Claims 8, 11, 16 and 17 drawn to a method of treating a patient for mixed anxiety-depression disorders.

5) Claims 8, 12, 16 and 17 drawn to a method of treating a patient for acute and chronic psychotic state.

6) Claims 8, 13, 16 and 17 drawn to a method of treating a patient for addiction to and withdrawal from a substance.

7) Claims 8, 14, 16 and 17 drawn to a method of treating a patient suffering from extra-pyramidal events induced by an anti-psychotic episode.

8) Claims 8, 15, 16 and 17 drawn to a method of treating a patient suffering from a symptomatic dimension during an acute or chronic psychotic state as an immunotherapy.

9) Claims 8, 13, 16 and 17 drawn to a method for preparing a medicament through the mixing the chemical compounds of formula with other additional pharmaceutically acceptable actives, recipients, fillers.

Applicants have provisionally elected with traverse the invention of Group I comprising claims 1 - 7 drawn to a method for the treatment of sleep disorders comprising the administration of 2-cyano-10-(2-methyl-3-methylamino)propyl)phenothiazine (also known as cyamemazine). Accordingly,

claims 1-7 are being examined and claims 8-20 are withdrawn from consideration since they are non-elected invention.

## I. Rejection under 35 U.S.C § 102

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by an article by Singer et al. (1973) entitled Clinical Effect of a Sedative Neuroleptic (Cyamemazine) as cited in an attached EMBASE abstract. It is asserted by the Examiner that Singer et al. teach 2-cyano-10-(2-methyl-3-(methylamino)propyl)phenothiazine (also known as cyamemazine) is mainly indicated for the treatment of insomnia. (abstract). (see claims 1-3) Singer et al. also teach 2-cyano-10-(2-methyl-3-(methylamino)propyl)phenothiazine (also known as cyamemazine) was used as a sedative narcoleptic agent in 20 males and 20 female psychiatric inpatients. (see claims 1-5). It is noted that the patient population to be treated is not defined by the instant claims because claims are drawn to treating sleep disorders in any patient. The rejection is respectively traversed for the following reasons.

Claim 1 has now been amended to limit the claimed invention herein to a method of treating a patient for sleep disorders selected from the group consisting of insomnia and sleep apnea comprising the oral or parenteral administration of a therapeutically effective amount of from about 10 mg. to about 300 mg. of 2-cyano-10-(2-methyl-3-(methylaminopropyl)phenothiazine (I) or a pharmaceutically acceptable salt thereof. As the Examiner correctly points out, nowhere in Singer et. al. (1973) is the oral or parenteral administration of the active pharmaceutical 2-cyano-10-(2-methyl-3-(methylaminopropyl)phenothiazine (I) or a pharmaceutically acceptable salt thereof in an amount of from about 10 mg. to about 300 mg.disclosed for the treatment of insomnia or sleep apnea.

A claimed inventive compound, composition or a therapeutic method of using the same is anticipated if the disclosure in a single reference places that compound, composition or method of treatment using same in the possession of the public. Each and every element of the claimed invention must be disclosed within the four corners of the prior art reference and any reference that lacks any claimed element thereof cannot be said to anticipate. *In re Paulsen* 30 F.3d 1475; 31 U.S.P.Q. 2nd 1671 (Fed. Cir. 1994). The reference must "clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without any need for picking, choosing, and combining various disclosures . . . ."

*Minn. Min. & Mfg. Co. v Johnson and Johnson Orthopedics Inc.*, 976 F.2d 1559; 24 U.S.P.Q. 2nd 1321 (Fed. Cir. 1992). The reference must therefore provide a degree of precision with respect to the specific compound or method of treatment claimed and absence from the reference of any claimed element negates a finding of anticipation. *Abbott Laboratories v. Geneva Pharmaceuticals, Inc.*, 182 F.3d.1315; 51 U.S.P.Q.2d 1307 (Fed. Cir. 1999). The rejection of claims 1 – 5 for anticipation under 35 U.S.C. § 102(b) should therefore be withdrawn.

II. **Rejection under 35 U.S.C. §103**

Claims 4, 6 and 7 are also rejected under 35 U.S.C. 103(a) as being unpatentable for obviousness over the Singer et al. (1973) abstract in that it is asserted by the Examiner that the reference teaches that 2-cyano-10-(2-methyl-3-(methylamino)propyl)phenothiazine (also known as cyamemazine) is mainly indicated for the treatment of insomnia, psychomotor agitation, and delirium. The Examiner also maintains that the abstract teaches that the drug is used as a sedative narcoleptic in patients with a secondary psychiatric condition. Therefore, it is asserted that it would have been obvious to one of ordinary skill in the art to employ cyamemazine for the treatment of insomnia related to another mental disorder because Singer et al. teaches that cyamemazine is mainly indicated for insomnia and delirium (mental disorder). It is also argued that Singer et al. illustrates the administration of cyamemazine to psychiatric patients to achieve a sedative narcoleptic effect. One of ordinary skill in the art would therefore not have been motivated to employ cyamemazine for insomnia related to other disorders, particularly a disorder relating to mental status in order to achieve its main indicated effective treatment of both insomnia and mental disorder. This rejection is also traversed for the following reasons.

It is not disputed that Singer et. al (1973) teaches and discloses that cyamemazine is an effective and well tolerated drug which is useful in the treatment of psychotic, and sometimes neurotic syndromes which include distress, anxiety, agitation or psychomotor excitability. However, as result thereof, there is no teaching or suggestion whatsoever of the use of the drug in the treatment of insomnia or other sleep disorders such as sleep apnea nor is there even any indication in the article

that there is a reasonable expectation of successfully treating insomnia or sleep apnea alone with this compound.

Furthermore, it is admitted by the Examiner that the Singer et al. (1973) abstract does not teach the specific amounts of 2-cyano-10-(2-methyl-3-(methylamino)propyl)phenothiazine set forth in original claim 6, the treatment of Insomnia when related to another mental disorder as recited in original claim 4 and the routes of administration recited in original claim 7. Claims 6 and 7 have now been cancelled and these limitations have now been incorporated in new, independent claim 1. The amounts of active agent to be employed and the routes of administration are not obvious because Singer et al. is silent in this regard and does not teach or suggest any dosage amounts, routes of administration or the main indications of treating insomnia, sleep apnea and/or insomnia and an underlying mental disorder. The rejection of claims 4, 6 and 7 for obviousness under 35 U.S.C. § 103 must there be respectfully be withdrawn.

Claim 5 has also been rejected under 35 U.S.C. 103(a) as being unpatentable for obviousness over the Singer et al. (1973) abstract and further in view of a second article *Sleep Apnea and Cardiovascular Abnormalities* by Tilkian (1978). The Examiner based this rejection in the assumption that the patient population being treated in claim 5 is **suffering** from obstructive sleep apnea. It is asserted that Singer et al. teaches that 2-cyano-10-(2-methyl-3-(methylamino)propyl)phenothiazine (also known as cyamemazine) is mainly indicated for the treatment of insomnia. (abstract). However, it is also admitted that whereas the Singer et al. (1973) abstract does not teach the treatment of obstructive sleep apnea, the Tilkian abstract teaches insomnia is a symptom of obstructive sleep apnea. (abstract). It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ cyamemazine for the treatment of obstructive sleep apnea patients having insomnia because cyamemazine is effective in treatment of insomnia as taught by Singer et al. and because insomnia is a symptom of obstructive sleep apnea. One would have been motivated to make such a modification in order to successfully treat obstructive sleep apnea by treating the symptom of obstructive sleep apnea, insomnia that is effectively treatable with cyamemazine in view of Singer et al. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

This rejection is also respectfully traversed for the same reasons set forth above. Newly amended independent claim 1 now recites the method of treating sleep disorders selected from the group consisting of insomnia and sleep apnea comprising the oral or parenteral administration of a therapeutically effective amount of from about 10 mg. to about 300 mg. of 2-cyano-10-(2-methyl-3-(methylaminopropyl)phenothiazine (I) or a pharmaceutically acceptable salt thereof. Claim 5 now depends from claim 1 and therefore comprises all of these newly amended limitations. As discussed above, Singer et al. (1973) does not render claim 1 anticipated or obvious and the mere combination of this article with Tilkian does not render claim 5 obvious for the same reasons. The rejection of claim 5 under 35 U.S.C. 103(a) as being unpatentable for obviousness must also be withdrawn.

Not withstanding the Examiners' rejections of claims 1 – 7, in light of the foregoing amendments to the claims and arguments as to their patentability, it is respectfully asserted that the remaining pending claims now recite patentable subject matter that is clearly distinguishable and an advance over the cited prior art. It is further respectfully requested that said rejections of the claims be withdrawn so that they might pass to allowance and issue. Should however, the Examiner still have some remaining issue(s) or concern(s), he is earnestly solicited to contact the undersigned attorney so that any un-resolved matter might be overcome and resolved. In the event the Examiner wishes to contact the undersigned regarding any matter, please call (collect if necessary) the telephone number listed below.

Applicants believe there are no fees due for this response. However, if the Examiner deems that fees are due, please charge these fees to Deposit Account No. **18-1982** for sanofi-aventis, U.S. LLC, Bridgewater, NJ. Please credit any overpayment to Deposit

Account No. **18-1982**. and thank your consideration and assistance in this matter.

Respectfully submitted,

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